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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/765,287	09/12/1997	CAMILLE LOCHT	960-25	5876

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EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	39

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/765,287	LOCHT ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- Th MAILING DATE of this communication appears on the cov r sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18-22,27-30 and 34-42* is/are pending in the application.

4a) Of the above claim(s) *36 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18-22 and 27-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 27, 2003, paper # 38 has been entered.

Applicants' Amendments

2. Acknowledgement is made of Applicants' amendments G filed 3/13/2003 paper number 36, which has been entered.

Status of the Claims

3. Claims 1, 7, 34 and 40 have been amended; new claim 42 has been added.

Claims 1-15, 18-22, 27-30 and 34-42 are pending. Claims 36 and 38 were withdrawn from consideration. Claims 1-15, 18-22, 27-30, 34, 35, 37 and 39-42 are under consideration.

Prior Citations of Title 35 Sections

4. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

5. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 has been submitted with this office action.

Rejection (s) Maintained

Claim Rejections - 35 USC § 103

6. The rejection of claims 1-15, 18-22, 27- 30 and 39 under 35 U.S.C. 103 (a) as obvious over Loosmore et al. (EP 453216) in view of Menozzi et al. (FEMS Microbiology Letters, 78:59-64, 1991) is maintained for the reasons set forth in the office action mailed 12/18/2001 (paper number 27).

Applicants argue that Loosmore et al. describe transcriptional fusion while the instant application describe a translational fusion. Applicants further argue that Menozzi et al. teach that the Fha protein is able to interact with heparin, however one skilled in the art reading Menozzi's article and Loosemore's would have not arrived at the claimed invention, since Loosemore's reference is not relevant.

Applicants' arguments have been carefully considered, but they are not persuasive. It is the examiner's position that it seems the applicants argue the references individually and argue limitations that are not recited in the claims.

In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants' argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., transcriptional vs. translational fusion) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The Examiner respectfully draws applicants' attention to columns 3 and 4 of Loosmore et al. specifically column 4, lines 20- 58, which teach a fusion protein comprising an amino acid sequence from Fha fused to an amino acid sequence from a protein distinct from Fha. Loosmore et al. teach Fhap/TOX, Fhap/PRN and TOXp/Fha, as well as a recombinant strain with kinetics and yields comparable to the wild type strains.

Applicants further argue that Loosmore et al. gene fusions do not code in any way for "fusion proteins comprising an amino acid sequence distinct from Fha". Applicants contend that Loosemore et al. is different from the claimed invention in that the fusion in Loosemore's disclosure is only made between a promoter and a coding sequence.

It is the examiner's position that Loosemore et al. recite in column 2, lines 14-18 " Accordingly, in one aspect, the present invention provides a hybrid pertussis gene, comprising a structural pertussis gene fused at an ATG start codon to be a native but autologous pertussis promoter". Column 2, lines 24-28 further recite, " The present invention further provides a strain of *Bordetella*, particularly *Bordetella pertussis*, which has been transformed by the hybrid gene and is capable of expression of a gene product of the structural pertussis gene". Contrary to applicants' arguments, the hybrid gene generated by Loosemore et al. qualifies as the fusion agent and the gene product expressed by Loosemore's pertussis structural gene qualifies as a " polypeptide heterologous with respect to Fha of *Bordetella.*

With regard to the reference of Menozzi et al. applicants acknowledge that the reference teaches the Fha-heparin interactions, but contend that it does not teach a fusion protein construct comprising a Fha moiety. The applicants ' argument has been carefully considered, but it is not persuasive. The reference of Menozzi et al. has been applied to indicate the art- known fact that

the Fha, for example of Loosemore et al., contains the heparin interaction site. The hybrid gene of Loosemore et al. expresses Fha that contains the heparin interaction site and is implicit in the disclosure of Loosemore et al. in light of what is well known in the art, as taught by Menozzi et al. Therefore the rejection based on the above references is proper under 35 U.S.C. 103 (a).

7. The rejection of claims 34, 35 and 37 under 35 U.S.C. 103 (a) over Loosmore et al. (EP 453216) in view of Menozzi et al. (FEMS Microbiology Letters, 78:59-64, 1991) and Locht et al. is maintained for reasons set forth in paragraph 11, page 5 of the office action mailed 9/26/2000 (paper no. 21).

Applicants' arguments have been fully considered, but are not persuasive.

Applicants' arguments concerning Loosmore et al. and Menozzi et al. have been addressed above (see paragraph 6 above).

Applicants further argue that there is nothing in Locht et al. that would have suggested making fusion protein with Fha moiety.

It is the examiner's position that applicants argue the references individually. The rejection was based on a 103 rejection using combination of three references. It is the combination of the references that render the claims obvious. The reference of Locht et al. teaches the immunogenicity of Fha when presented to the mucosal immune system. Given this disclosure, it would have been obvious to one of ordinary skill in the art at time the invention was made to present Loosmore's composition as modified by Menozzi et al. to the mucosal immune system to produce the instant invention, as set forth on page 7 of the action in paper number19, one of ordinary skill in the art would have been motivated to produce the instant invention in order to achieve effective and long lasting local or mucosal immunity as taught by Locht et al.

8. The rejection of claims 40-41 under 35 U.S.C. 102(e) as anticipated by by Relman et al. is maintained.

The rejection was stated as below:

Claims 40-41 are drawn to the host cells belonging to a bacterial species other than *Bordetella.*

Relman et al. disclose host organisms or strains from pathogens other than *Bordetella.* They disclose other organisms such as *E. coli, Salmonella, Yersinia* or *Pseudomonas* (see column 4, lines 44-48) expressing a fusion protein or hybrid protein comprising a part of the filamentous haemagglutinin or Fha and a part of a protein heterologous to Fha. They disclose seven portions of the Fha B open reading frame were each cloned into the expression vector (see column 9).

Relman et al. disclose that nucleic acid and protein compositions are provided from *B. pertusis*, which may find use in diagnosis and treatment of disease. Particularly they disclose that an open reading frame encoding filamentous hemagglutinin precursors provided, with the intact protein for the filamentous hemagglutinin portion thereof can be expressed in a wide variety of hosts including *E. coli*, for use in the production of antibodies, for immunodiagnosis or therapy, or as vaccine for prophylactic purposes. (see abstract and claims).

Applicants' arguments have been fully considered, but are not persuasive.

Applicants argue " The examiner refers to column 9 of Relman et al. which discloses Fha B fusion proteins. Applicants refer to the same column, especially lines 45-59. This paragraph indeed discloses fusion proteins between part of the Fha and the phage MS2 RNA polymerase.

However contrary to the fusion recited in claim 40, these fusion proteins have an N-terminal moiety constituted by the " first 98 amino acids of the phage MS2 RNA polymerase" and a C-terminal moiety consisting of Fha C-terminal fragment". Applicants further submit that "the fusion protein described by Relman et al. comprise a N-terminal moiety from MS2 and a C-terminal moiety corresponding to a fragment o f FHA". Applicants further argue although one fusion comprises the N-terminal extremity of Fha, this fragment is still in the C-terminal portion of the corresponding fusion protein. Applicants later recites some references.

It is the examiner's position that applicants argue limitations that are not recited in the claims.

It is the examiner's position that Relman et al. do not only teach a C-terminal Fha moiety but also teach a N-terminal moiety consisting of Fha N-terminal fragment (see column 2, lines 30-35, and claims 8-10). The prior art still anticipates the amended claims.

New Ground for Rejections

Claim Rejections - 35 USC § 112

9. Claims 1 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

Amended claims 1 and 34 are rejected under 112 1st paragraph because of the deletion of the limitation of " said sequence (2), when placed under the control of a promoter recognized by the cellular polymerases of *B. pertussis* and introduced into a *B. pertussis* cell culture is

expressed in this culture and excreted into the culture medium of these cells or exposed at the surface of these cells, wherein said recombinant DNA when expressed produces highly immunogenic fusion proteins". This deletion now broadens the scope of the claims since the sequence is not required to be placed under the control of a promoter recognized by the cellular polymerases of *B. pertussis* and therefore raise new issues under 35 USC 112.

Therefore the amendment of the claims are considered **new matter**. *In re Rasussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step or a compound from a disclosure. See MPEP 608.04.

Applicants are respectfully requested to remove the new matter from the claims.

Claim Rejections - 35 USC § 102(e)

10. Newly added claim 42 is rejected under 35 U.S.C. 102(e) as anticipated by Relman et al. For the details see paragraph 8 above. Added claim 42 recites the same limitation as the original claim 40, which was rejected under 35, U.S.C. 102(e) as anticipated by Relman et al.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

September 17, 2003

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER